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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/625,260	07/22/2003	Philip J. Gotwals	A073-USCN2	4395

7590 06/17/2004

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/625,260	GOTWALS ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16 and 18-22* is/are rejected.

7)☐ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 15-23 are pending.

2. Applicant's election of Group V, claim 15-22 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claim 23 is withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. The specification on page 1 should be amended to reflect the status of parent application No. 10/061,658.

The U.S. Patent 6,652,856 cited on the PTO FORM 892 is issued from the parental application serial No. 10/061,658 and will not be supplied.

5. Applicant's IDS, filed 7/22/04, is acknowledged, however, references EG-EL were crossed out as the entire documents were not found. Applicant is invited to produce such documents.

6. The ATCC deposit information in conjunction with Applicant's statement, filed 5/21/03 in parent application No. 10/061,658, are sufficient to satisfy the deposit of biological materials of the hybridoma ATCC PTA-3580 that produce the AJH10 antibody under 35 U.S.C. § 112, first paragraph.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 21-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "an amino acid sequence that is equivalent or homologous to such sequence" claimed in claims 21-22, lines 3-4 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 7-22-03 does not point to the specification for support for the newly added limitations "an amino acid sequence that is equivalent or homologous to such

sequence" as claimed in claims 21-22. However, the specification does not provide a clear support of such limitation. The instant claims now recite a limitation, which was not clearly disclosed in the specification and recited in the claims as originally filed.

9. Claims 15-16 and 18-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treatment or inhibiting rheumatoid arthritis comprising administering to a subject anti-α1β1 integrin antibody, does not reasonably provide **enablement** for a method for treatment of rheumatoid arthritis comprising administering to a subject anti-α1β1 integrin "fragment" in claim 15, or a method for "preventing" rheumatoid arthritis comprising administering to a subject anti-α1β1 integrin antibody or "fragment thereof" in claim 16, wherein the antibody is an anti-α1-I domain blocking antibody and the amino acid sequence of the antibody epitope comprises the sequence of SEQ ID NO:8 or "an amino acid sequence that is equivalent or homologous to such sequence" in claims 21-22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Besides, SEQ ID NO:8 epitope, the specification is silent with respect to specifically which amino acids are critical to the claimed α1β1 antibody in the method for treating RA such that one skilled in the art could predict which α1β1 integrin "fragments"; or "equivalent" or "homolog" of epitope comprising SEQ ID NO: 8 would fall within the scope of the claims to be used in the method of inhibiting/treating RA.

There is insufficient guidance and direction as to what is the nature of the structural and functional constraints on the claimed "equivalent or homologs" and, in turn, what is the predictability of making and using such "equivalent or homologs" in a manner consistent with the disclosed method for treatment of RA. The "equivalent or homologs" epitopes encompassed by the claimed invention would be expected to have varying degrees of inhibitory activity on adhesion of α1β1 and of these only certain ones would be predictive of in vivo inhibitory qualities encompassed by the claimed invention. Colman *et al* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding.

Applicant's fragment of the "α1β1 integrin" protein includes any fragment. Applicant has not provided sufficient information or guidance to indicate which fragments which encompass epitopes that are useful for generating antibodies with the claimed functional properties

On the basis of the disclosed correlation of the anti-fibrotic treatment and the tendency of reducing BL-induced lung collagen accumulation in mice observation alone, applicant concludes that the scope of the antibody against α1β1 encompassed by the claimed invention can have biological activity to prevent the RA and be provided as pharmaceutical compositions to subjects including human to effectively prevent RA. It is unclear which patients would be candidates for

in vivo prevention with antibodies to α1β1 integrin. In addition, although such antibodies were to redyce BL-induced lung collagen accumulation in mice, it is unclear if these assay results are predictive of a method for preventing RA comprising administering the antibody that immunoreacts with α1β1.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Claims 15-16 and 18-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method for treatment or inhibiting rheumatoid arthritis comprising administering to a subject anti-α1β1 integrin antibody.

Applicant is not in possession of a method for treatment of rheumatoid arthritis comprising administering to a subject anti-α1β1 integrin "fragment" in claim 15, or a method for "preventing" rheumatoid arthritis comprising administering to a subject anti-α1β1 integrin antibody or "fragment thereof" in claim 16, wherein the antibody is an anti-α1-I domain blocking antibody and the amino acid sequence of the antibody epitope comprises the sequence of SEQ ID NO:8 or "an amino acid sequence that is equivalent or homologous to such sequence" in claims 21-22.

Applicant has disclosed only antibody to α1β1 integrin comprising SEQ ID NO: 8; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

12. Claims 15-16 and 19-22 rejected under 35 U.S.C. 102(e2) as being anticipated by US. Pat. No. 5,855,888.

The `888 patent teaches a method for treating rheumatoid arthritis comprising administering to a patient an anti-VLA-1 ($\alpha 1\beta 1$) antibody (see col., 4-5 under Experiment 1, table 1 and patented claims 1-6 in particular). The `888 patent teaches that the antibody used for the RA treating drug can inhibit the swelling due to arthritis in RA, specially mAb that recognize the extracellular region of adhesion molecule of human VLA family (see col., 4, lines 39-46 in particular). The `888 patent further teaches that the antibody can be chimeric antibody (col., 3, lines 42-46), humanized antibody (col., 3, line 59) or monoclonal (see col., 4, lines 62-65). Furthermore, the patented anti-VLA-1 antibody recognizes an epitope on VLA-1 protein which comprises claimed SEQ ID NO: 2. The term "comprises" in claims 21-22 is open-ended so that the epitope may include additional amino acids on either or both of the N- or C- termini of given sequence.

The reference antibody comprise antigen binding regions derived from the light and heavy chain variable regions of $\alpha 1\beta 1$.

The reference teachings anticipate the claimed invention.

13. Claims 15-16 and 19-22 are rejected under 35 U.S.C. 102(e2) as being anticipated by U.S. Patent No. 5,788,966.

The `966 patent teaches a method for treating arthritis (see the entire document and column 10, patented claims 1-8 and column 8 lines 65-67 in particular) such as rheumatoid arthritis (see col., 3 lines 64-65 in particular) that is associated with elevated levels of VLA-1 comprising administering to a human a monoclonal antibody 1B3.1 or a fragment thereto (column 3 lines 5-10) that inhibits collagen binding to VLA-1 (see entire document and reference claims 1-8, column 10 in particular). Furthermore, the `966 patent teaches that IB3.1 antibody recognizes an epitope on VLA-1 protein (see column 8 lines 39-46 in particular). The term "comprises" in claims 21-22 is open-ended so that the epitope may include additional amino acids on either or both of the N- or C- termini of given sequence.

The reference antibody comprise antigen binding regions derived from the light and heavy chain variable regions of $\alpha 1\beta 1$.

The reference teachings anticipate the claimed invention.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 15-16 and 19-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 09/996,738. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are expressly claiming the same subject mater, although they differ in scope. While the `738 application is claiming a specific dosing and specific percentages decrease in the arthritic score. It has been held that where the general conditions of a claim are disclosed in the prior art , discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II. Further, the recited percentages of inhibition of

arthritic score is considered an inherent property of the anti-α1β1 antibody. Both applications are drawn to the same method of treating rheumatoid arthritis using anti-VLA-1 antibody.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. Claims 15-16 and 19-22 are directed to an invention not patentably distinct from claims 1-7 of commonly assigned 09/996,738. Specifically, both applications are drawn to the same method of treatment of rheumatoide arthritis comprising administering to the subject an antibody to the α1β1 integrin. Therefore, they are not patentably distinct.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 09/996,738, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

17. Claim 17 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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